UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

EXAMINER
[illegible]

ART UNIT	PAPER NUMBER
[illegible]	19

DATE MAILED: [illegible]

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/914,332	Van Arsdell et al.
Examiner	**Group Art Unit**
Peter Tung	1652

☐ Responsive to communication(s) filed on _____ .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-31* is/are pending in the application.

Of the above, claim(s) *23-31* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, and 5-22* is/are rejected.

☒ Claim(s) *3 and 4* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 11 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is explained in the Office action dated 2/1/99.

3. Applicants argue that the strains in question have been deposited with the ATCC and that one of ordinary skill in the art would be able to obtain and use a bacterium with a deregulated KAPA-to-DAPA biosynthetic pathway.

4. Applicant's arguments filed 12/20/99 have been fully considered but they are not persuasive. While the specific DNAs have been provided, the specification still does not provide sufficient teaching on deregulating the KAPPA-to DAPPA biosynthetic step. It is not clear where the *bio* locus is disrupted by the DNA cassettes as the *bio* locus also includes *bioA*. Additionally, the instant claims are drawn to a bacterium with a deregulated biotin biosynthetic pathway while the examples provided in the specification are for a lysine biosynthetic pathway.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 2, 5-7 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy-Schil et al. Levy-Schil et al. teach (page 755, "Bacterial strains and media," "Biotin and vitamer quantification") a method of making biotin by culturing *E. coli* in a medium comprising casamino acids and purifying the biotin produced. Casamino acids comprise lysine and aspartate, a lysine precursor. Additionally, the *E. coli* of the instant reference does not teach that the SAM-utilizing DAPA aminotransferase is not capable of using lysine. Levy-Schil et al. do not teach adding casamino acids to a concentration of at least 10 mMolar. It would have been obvious to one of ordinary skill in the art at the time the invention was made to culture the biotin producing

E. coli in a medium of at least 10 mMolar for the benefit of providing sufficient nutrients (i.e. casamino acids) for growing large amounts of E. coli and increasing biotin production. One of ordinary skill would have a reasonable expectation of success at doing this as supplementing or increasing nutrients for fermentative growth is well known in the art. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

7. Applicants argue that Levy-Schil et al. does not teach a microorganism where the DAPA aminotransferase is able to use lysine. Additionally, the reference does not teach culturing using at least 10 mmoles per liter of lysine, a lysine analog or a lysine precursor.

8. Applicant's arguments with respect to claims 1, 2, 6, 7 and 12 have been considered but are moot in view of the new ground(s) of rejection. While the reference does not state that the DAPA-aminotransferase is able to use lysine, there is no teaching that lysine cannot be used by the DAPA-aminotransferase.

9. Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy-Schil et al. in view of Yamada et al. (U.S. Patent No. 4,563,426). The teachings of Levy-Schil et al. have been discussed supra. Claim 8 adds the further limitation of converting the recovered dethiobiotin to biotin by a separate process. Levy-Schil et al. further teach (page 755, "Bacterial strains and media," "Biotin and vitamer quantification") a method of making dethiobiotin by culturing *E. coli* in a medium comprising casamino acids and purifying the dethiobiotin produced. Levy-Schil et al. do not teach converting dethiobiotin to biotin by a separate process. Yamada et

al.(U.S. Patent No. 4,563,426) teach (column 1, lines 40-66) a method of producing biotin by adding dethiobiotin to a fermentation medium. Yamada et al. do not teach dethiobiotin production. It would have been obvious to one of ordinary skill in the art at the time the invention was made to convert the dethiobiotin produced as taught by Levy-Schil et al., into biotin as taught by Yamada et al., for the benefit of producing biotin. One of ordinary skill in the art is motivated to combine the teachings as Levy-Schil et al. show a method of making dethiobiotin and the teachings of Yamada et al. show how to produce biotin from dethiobiotin. One of ordinary skill in the art would have a reasonable expectation of success at doing this as the teachings of Levy-Schil et al. show a method of making dethiobiotin, which is a starting material for making biotin, as shown by the teachings of Yamada et al. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

10. Applicants argue that Yamada et al. or Levy-Schil et al. do not teach a microorganism where the DAPA aminotransferase is able to use lysine. Additionally, the reference does not teach culturing using at least 10 mmoles per liter of lysine, a lysine analog or a lysine precursor.

11. Applicant's arguments with respect to claims 1 and 8 have been considered but are moot in view of the new ground(s) of rejection. While the references do not state that the DAPA-aminotransferase is able to use lysine, there is no teaching that lysine cannot be used by the DAPA-aminotransferase.

12. Claims 1, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy-Schil et al. in view of Komatsubara et al. (U.S. Pat. No. 5,374,554). The teachings of Levy-Schil

et al. have been discussed supra. Claims 9 and 10 add the further limitation of a bacterium resistant to the lysine analog S-2-aminoethyl-L-cysteine. Levy-Schil et al. do not teach a bacterium resistant to the lysine analog S-2-aminoethyl-L-cysteine. Komatsubara et al. (U.S. Pat. No. 5,374,554) teach a *Serratia* strain resistant to S-2-aminoethyl-L-cysteine which is used for biotin production. The *Serratia* would be expected to inherently comprise a lysine-utilizing DAPA aminotransferase. Komatsubara et al. do not teach using lysine or a lysine precursor in the growth media for said *Serratia* strain for the production of biotin. It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce biotin using the Serratia strain resistant to S-2-aminoethyl-L-cysteine, as taught by Komatsubara et al. using the growth media taught by Levy-Schil et al. for the benefit of growing the Serratia in a rich medium. One of ordinary skill in the art is motivated to do this as a rich medium would provide extra nutrients and allow the faster growth of the bacteria. One of ordinary skill in the art has a reasonable expectation of success at doing this as bacteria are grown in many different media and the use of a rich medium (casamino acids are provided) to improve the growth of bacteria is well known in the art. As casamino acids comprise lysine and aspartate, a lysine precursor, the limitations of claim 1 are anticipated. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

13. Applicants argue that Komatsubara or Levy-Schil et al. do not teach a microorganism where the DAPA aminotransferase is able to use lysine. Additionally, the reference does not teach culturing using at least 10 mmoles per liter of lysine, a lysine analog or a lysine precursor.

14. Applicant's arguments with respect to claims 1, 9 and 10 have been considered but are moot in view of the new ground(s) of rejection. While the references do not state that the organism comprises a DAPA-aminotransferase which is able to use lysine, there is no teaching to the contrary.

Allowable Subject Matter

15. Claims 3, 4 and 13-22 are allowable over the prior art of record. The prior art of record does not teach or suggest a method of making biotin using an overproducer of lysine-utilizing DAPA aminotransferase or also expressing additional SAM-utilizing DAPA aminotransferase.

16. Claims 3 and 4 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

17. No claims are allowed.

Conclusion

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, Ph.D., can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600